FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, LIFESCI' ENTERED AT 09:06:58 ON 24 MAR 2005

L5 20 S BMPR1A AND KNOCKOUT

L6 12 DUP REM L5 (8 DUPLICATES REMOVED)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	8052	nuclear same transfer	US-PGPUB; USPAT	OR	OFF	2005/03/24 11:55
L2	85356	l1 or cloning	US-PGPUB; USPAT	OR	OFF	2005/03/24 11:55
L3	31348	l2 and (transgenic or knockout)	US-PGPUB; USPAT	OR	OFF	2005/03/24 11:55
L4	3	l3 and (lineage adj deficient)	US-PGPUB; USPAT	OR	OFF	2005/03/24 12:07
L5	3	l2 and (lineage adj deficient)	US-PGPUB; USPAT	OR	OFF	2005/03/24 12:07
L6	0	l5 not l4	US-PGPUB; USPAT	OR	OFF	2005/03/24 12:07

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, LIFESCI' ENTERED AT 08:05:53 ON 24 MAR 2005

L1 3773 S SMAD2
L2 103 S L1 AND KNOCKOUT
L3 6 S L2 AND MESODERM
L4 2 DUP REM L3 (4 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, LIFESCI' ENTERED AT 09:06:58 ON 24 MAR 2005

=> d bib ab 1 2

L4 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
AN 2002627069 MEDLINE
DN PubMed ID: 12384562
TI Compound disruption of **smad2** accelerates malignant progression of intestinal tumors in apc **knockout** mice.
AU Hamamoto Toshiaki; Beppu Hideyuki; Okada Hitoshi; Kawabata Masahiro; Kitamura Tadaichi; Miyazono Kohei; Kato Mitsuyasu
CS Departments of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo 170-8455, Japan.
SO Cancer research, (2002 Oct 15) 62 (20) 5955-61.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20021018
Last Updated on STN: 20021214
Entered Medline: 20021129
AB **Smad2** is a receptor-regulated Smad that is activated specifically by transforming growth factor beta and activin signaling. We disrupted the mouse **Smad2** gene by gene targeting. Homozygous **Smad2** mutant mice died around E8.5 with impaired visceral endoderm function and deficiency of **mesoderm** formation. Heterozygotes were fertile and had no apparent abnormality up to at least 1 1/2 year of age. To examine the role of **Smad2** inactivation in the process of carcinogenesis, we prepared compound heterozygous mice, which carry both Apc and **Smad2** mutations on the same chromosome in the cis-configuration. Compound inactivation of **Smad2** in heterozygous Apc mutant mice did not change the total number of intestinal tumors but increased sudden death from intestinal obstruction caused by extremely large tumors. Furthermore, histological examination revealed that Apc/**Smad2** cis-compound heterozygotes developed multiple invasive cancers that had never been observed in Apc single heterozygotes. These results indicate that loss of **Smad2** does not initiate tumorigenesis by itself but accelerates malignant progression of tumors to invasive cancer in the late stages of carcinogenesis.

L4 ANSWER 2 OF 2 MEDLINE on STN
AN 2001267879 MEDLINE
DN PubMed ID: 11358869
TI FoxH1 (Fast) functions to specify the anterior primitive streak in the mouse.
AU Hoodless P A; Pye M; Chazaud C; Labbe E; Attisano L; Rossant J; Wrana J L
CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada M5G 1X5.
SO Genes & development, (2001 May 15) 15 (10) 1257-71.
Journal code: 8711660. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB The node and the anterior visceral endoderm (AVE) are important organizing centers that pattern the mouse embryo by establishing the anterior-posterior (A-P), dorsal-ventral (D-V), and left-right (L-R) axes. Activin/nodal signaling through the **Smad2** pathway has been implicated in AVE formation and in morphogenesis of the primitive streak, the anterior end of which gives rise to the node. The forkhead DNA-binding protein, FoxH1 (or Fast), functions as a Smad DNA-binding partner to regulate transcription in response to activin signaling. Here, we show that deletion of FoxH1 in mice results in failure to pattern the anterior primitive streak (APS) and form node, prechordal **mesoderm**, notochord, and definitive endoderm. In contrast, formation of the AVE can occur in the absence of FoxH1. The FoxH1 mutant phenotype is remarkably similar to that of mice deficient in the forkhead protein Foxa2 (HNF3beta), and we show that Foxa2 expression is dependent on FoxH1 function. These results show that FoxH1 functions in an activin/nodal-Smad signaling pathway that acts upstream of Foxa2 and is required specifically for patterning the APS and node in the mouse.